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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,618	06/26/2003	Ralph C. Judd	UM/SBC147BUSA	4915

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,618	JUDD ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,30-36,39-46 and 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,30-36,39-46 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *061207*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Applicants' Amendment

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 06/12/07 in response to the non-final Office Action mailed 12/15/06.

Status of Claims

2) Claims 21 and 37 have been canceled via the amendment filed 09/21/07.

Claims 25, 30, 33, 44 and 50 have been amended via the amendment filed 09/21/07.

Claims 25, 30-36, 39-46 and 50-52 are pending and are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' Information Disclosure Statement filed 06/12/07. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

6) The rejection of claim 21 and those dependent therefrom made in paragraph 36 of the Office Action mailed 12/15/06 under 35 U.S.C § first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of claim 21.

7) The rejection of claim 21 made in paragraphs 39(a) and 39(b) of the Office Action mailed 12/15/06 under 35 U.S.C § second paragraph, as being indefinite, is moot in light of Applicants' cancellation of claim.

8) The rejection of claims 21 and 37 made in paragraph 40 of the Office Action mailed 12/15/06 under 35 U.S.C § 102(e)(2) as being anticipated by Rubenfield *et al.* (US 6,551,795,

filed 02/18/1998, already of record) as evidenced by Harlow *et al.* (*In*: *Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record), is moot in light of Applicants' cancellation of claims.

9) The rejection of claim 21 made in paragraph 41 of the Office Action mailed 12/15/06 under 35 U.S.C § 102(b) as being anticipated by Manning *et al.* (*Microb. Pathogenesis*. 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998) in light of Richarme *et al.* (*Ann. Microbiol.* 133A: 199-204, 1982, already of record), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

10) The rejection of claim 50 and those dependent therefrom made in paragraph 36 of the Office Action mailed 12/15/06 under 35 U.S.C § first paragraph, as containing new subject matter, is withdrawn. A new/modified rejection is set forth below to address the claim, as amended. Applicants' pertinent arguments are addressed therein

11) The rejection of claim 34 and those dependent therefrom made in paragraph 37 of the Office Action mailed 12/15/06 under 35 U.S.C § first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claims 25 and 50 made in paragraph 39(c) of the Office Action mailed 12/15/06 under 35 U.S.C § second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

13) The rejection of claim 34 made in paragraph 39(d) of the Office Action mailed 12/15/06 under 35 U.S.C § second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claims 25, 30-36 and 39-46 made in paragraph 40 of the Office Action mailed 12/15/06 under 35 U.S.C § 102(e)(2) as being anticipated by Rubenfield *et al.* (US 6,551,795, filed 02/18/1998, already of record) as evidenced by Harlow *et al.* (*In*: *Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record), is withdrawn in light of Applicants' amendment to the claims.

Rejection(s) Maintained

15) The rejection of claims 43 and 51 made in paragraph 38 of the Office Action mailed 12/15/06 under 35 U.S.C § first paragraph, as containing new subject matter, is maintained for the reasons set forth therein and herein below.

Applicants contend that the specification discusses the 'substantial similarity' of these two proteins in both amino acid sequence and structure, particularly at the N termini of both proteins, and even designates both proteins by the same name. Applicants state that given this a person of skill in the art would clearly understand that the signal sequence of one such protein is a signal sequence of the other. The differences in the two sequences, both at the amino acid sequence and the gross structural level, would not be considered by one of skill in the art to change the function of the signal sequence from one OMP85 protein to the other. Applicants cite MPEP § 2163 and state that the newly added claim limitations can be implicitly or inherently supported in the specification as well as by express disclosure. Applicants state that column 2 at pages 2100-183 of MPEP § 2163 provides that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the 'reference' and that it would be so recognized by persons or ordinary skill. Applicants assert that the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, Applicant was in possession of the invention now claimed. Applicants submit that there is no reason why a person of skill in the art would not recognize the support in the disclosure for all of the claim language, including that the signal sequence of the OMP85 from *Neisseria gonorrhoeae* in the identical position in the structurally 'similar' OMP85 protein of *Neisseria meningitidis*, was a signal sequence, particularly given the remaining description of these proteins throughout the specification. Applicants allege that the Office has not provided such reasoning. Applicants submit that one of skill in the art would understand that the signal sequence identified in Figure 2 for SEQ ID NO: 2 is identical and in the identical position in the homologous OMP85 protein of SEQ ID NO: 4. Applicants assert that the identification of that signal sequence and cleavage site in SEQ ID NO: 2 is inherent for the same sequence and cleavage site in SEQ ID NO: 4. Applicants conclude that one of skill in the art given the present disclosure would find inherent support for the claim language of claims 43 and 51.

Applicants' arguments have been carefully considered, but are not persuasive. The designation of two structurally non-identical proteins by one name is not sufficient to overcome the new matter rejection of record. The two proteins are not structurally 'identical' at the N-termini as admitted by Applicants in the second full paragraph of page 6 and first full paragraph on page 9 of their 'Remarks/Arguments' filed 06/12/07. A signal peptide-lacking polypeptide having 95%, 96%, 97%, 98%, 99% or 100% sequence identity with the 797 amino acid-long SEQ ID NO: 4 and concurrently having the ability to induce antibodies in a mammalian patient wherein the antibodies bind to SEQ ID NO: 4 and having the capacity to interfere with the ability of *Neisseria gonorrhoeae* to adhere to mammalian epithelial cells in a gonococcal cell adherence assay, has no descriptive support in the instant specification as filed. As set forth previously, Figure 2 depicts SEQ ID NO: 2. Figure 5 documents that the amino acid sequence of SEQ ID NO: 4 is non-identical to the amino acid sequence of SEQ ID NO: 2 in amino acid composition and in length. The amino acid sequence of SEQ ID NO: 4 is 797 amino acids in length, whereas the amino acid sequence of SEQ ID NO: 2 is 792 amino acids in length. The N-terminal halves of the two proteins are not identical. More than 30 amino acid residues are *different* in these two full length polypeptide sequences. See Figure 5. The signal peptide that is identified in Figure 2 as filed is of the gonococcal Omp85 having the amino acid sequence of SEQ ID NO: 2, not of the structurally non-identical meningococcal Omp85 having the amino acid sequence of SEQ ID NO: 4. The Figure 2 descriptions are limited to SEQ ID NO: 2. The reference recited therein of von Heijne (*Nucl. Acids Res.* 14: 4683-4690, 1986) does not identify the signal peptide of an amino acid sequence having 95%, 96%, 97%, 98%, 99% or 100% sequence identity with SEQ ID NO: 4, or the signal peptide of any gonococcal, meningococcal, or neisserial polypeptide to be spanning amino acids 1-21 of SEQ ID NO: 4. Given the structural heterogeneity among OMP85 proteins, the identification of the signal sequence and cleavage site in SEQ ID NO: 2 does not inherently and necessarily support the same signal sequence and cleavage site in the structurally non-identical and much longer SEQ ID NO: 4. The upto 5% non-identity in the recited polypeptide includes and does not exclude variations or non-identity within the signal peptide. No part of the specification provides the descriptive support for an immunogenic polypeptide comprising an amino acid sequence having 95%, 96%, 97%, 98%, 99% or 100% sequence identity with SEQ ID NO: 4 and lacking 1-21 amino acids of SEQ ID NO: 4 as recited in claim 43 or 51, which signal peptide-

lacking polypeptide induces antibodies in a mammalian patient that bind to SEQ ID NO: 4 and that interfere with the ability of *Neisseria gonorrhoeae* to adhere to mammalian epithelial cells in a gonococcal cell adherence assay. Note that the antibodies that interfere with the ability of *Neisseria gonorrhoeae* to adhere to Chang epithelial cells in a gonococcal cell adherence assay were produced using the first 178 amino acids of SEQ ID NO: 2 (see Example 8) which *includes* the signal peptide, and which is non-identical in amino acid composition to the first 178 amino acids of SEQ ID NO: 4. With or without a 21 amino acid-long signal peptide, the first 178 amino acids of the 792 amino acid-long SEQ ID NO: 2 (differing in three amino acids compared to the first 178 amino acids of the 797 amino acid-long SEQ ID NO: 4) do not and cannot provide support for an amino acid sequence having 95%, 96%, 97%, 98%, 99% or 100% sequence identity with the 797 amino acid-long sequence of SEQ ID NO: 4. The antibodies described in Example 7 are produced using the first 200 amino acids of the gonococcal SEQ ID NO: 2 which *includes* the signal peptide and which is non-identical in amino acid composition to the first 200 amino acids of SEQ ID NO: 4. Contrary to Applicants' assertion, the identified limitations are neither supported inherently nor implicitly in the specification or by express disclosure. The specification does not convey with reasonable clarity to those skilled in the art, that as of the filing date sought, Applicant was in possession of the invention now claimed. Contrary to Applicants' assertion, the Office has provided sufficient reasoning in support of the rejection. The specification does not convey with reasonable clarity that Applicants had possession of the claimed invention. The rejection of record stands.

16) The rejection of claims 25, 31-36, 39-42, 44-46, 50, 52 and 53 are rejected under 35 U.S.C § 102(b) as being anticipated by Manning *et al.* (*Microb. Pathogenesis.* 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998) in light of Richarme *et al.* (*Ann. Microbiol.* 133A: 199-204, 1982, already of record), is maintained for the reasons set forth therein and herein below.

Applicants contend that the pending claims do not introduce new matter, but are fully supported by the specification, which is a continuation of the prior application 09994192, filed 11/26/01, which is a continuation of the prior application 09/177,039, filed 10/22/1998. Applicants state that except for minor formal and grammatical corrections, these applications have the same specifications.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth herein above and below, the new matter rejections are still pending. Therefore, the instant claims are granted the effective filing date of the instant specification, i.e., 06/26/03. The reference of Manning *et al.* (1998) is maintained as an anticipatory reference.

New Rejection(s) Necessitated by Applicants' Amendments

17) Claim 50 and those dependent therefrom are rejected under 35 U.S.C § first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 50 is now amended to indicate that the antibodies induced by the immunogenic composition comprising an isolated polypeptide comprising an amino acid sequence having 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4 interfere with the ability of '*Neisseria gonorrhoeae* bacteria to adhere to mammalian epithelial cells in a gonococcal cell adherence assay'. Applicants point to lines 26-29 of page 20; lines 25-30 of page 25; page 26, line 14 through page 27, line 2; lines 7-10 of page 35; and in Example 8 at page 53 of the specification. Applicants state that the antiserum used in Example 8 was developed to the first 178 amino acids of SEQ ID NO: 2, which differ from the first 178 amino acids of SEQ ID NO: 4 only by three amino acids, and therefore make the following conclusion:

> Thus the polypeptide used to immunize the mammalian subjects of the preceding examples falls within the claim language "an isolated polypeptide having 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4".

However, the amino acid sequence of SEQ ID NO: 4 is 797 amino acids in length. The first 178 amino acid-long sequence from SEQ ID NO: 2, differing in three amino acid residues with the first 178 amino acid-long sequence of the full length SEQ ID NO: 4, does not constitute an amino acid sequence having 95% or greater sequence identity with the 797 amino acid-long sequence of SEQ ID NO: 4. 178 residues do not constitute 95% of 797 residues. The 5% non-identity in the recited polypeptide includes and does not exclude variations or non-identity within the signal peptide. Furthermore, the limitation in claim 50, 'an amino acid sequence having 95% or greater sequence identity with ..... SEQ ID NO: 4', encompasses amino acid sequence species having 95%, 96%, 97%, 98% and 99% sequence identity with SEQ ID NO: 4 and concurrently having the ability to induce antibodies in a mammalian patient that bind to SEQ ID NO: 4 and the capacity to interfere

with the ability of *Neisseria gonorrhoeae* bacteria to adhere to mammalian epithelial cells in a gonococcal cell adherence assay. The instant specification as filed does not have descriptive support for these sequence species having each of the recited functional characteristics.

Applicants further state that they have identified the mammalian cells exemplified in the assay as 'epithelial' cells based on use of the well known Chang human epithelial cell model, which is a frequently used model cell line representative of mammalian epithelial cells. Applicants cite Makino *et al.* and Duensing *et al.* as two examples of publications evidencing the use of the model mammalian epithelial cell line. However, the description of one mammalian epithelial cell species, i.e., Chang epithelial cell species, used in the gonococcal cell adherence assay of Example 8 does not provide descriptive support for the genus limitation 'mammalian epithelial cells' in a gonococcal cell adherence assay. The only mammalian epithelial cell species used in the gonococcal cell adherence of Example 8 are --Chang epithelial cells--. The newly introduced amendment renders the scope of the claim(s) broader than the original disclosure.

Applicants submit that the term 'mammalian patient' or subject is supported by the use of a model mammalian patient in the generation of the antibodies used in Examples 7 and 8, and in the disclosure of the specification referring to 'mammals' at page 1, line 17. However, Example 8 describes an *in vitro* assay, but does not provide support for inducing antibodies in any mammalian 'patient'. Example 7 describes the production of polyvalent antisera produced in one mammalian species, rabbits, using a fusion protein in which the first 200 amino acids of the gonococcal Omp85 (SEQ ID NO: 2) were genetically fused to maltose binding protein (MBP). The rabbits are not described herein as 'patients' suffering from any disease. Example 8 describes a rabbit antiserum to the first 178 amino acids of SEQ ID NO: 2. These two examples and line 17 of page 1 do not provide descriptive support for a rabbit patient, let alone a 'mammalian patient'. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the new limitation(s), or remove the new matter from the claim(s).

Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

18) Claims 25 and 39-46 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 25, as amended, is indefinite and incorrect in the limitation 'an isolated polypeptide of claim 50', because claim 50 is not drawn to 'an isolated polypeptide', but to 'an immunogenic composition' comprising a pharmaceutically acceptable carrier and an isolated polypeptide as recited therein.

(b) Claims 39-46, which depend directly or indirectly from claim 25, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Remarks

19) Claims 25, 30-36, 39-46 and 50-52 stand rejected.

20) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Central Fax number (571) 273-8300, which receives facsimile transmissions 24 hours a day and 7 days a week.

22) Information regarding the status of an application may be obtained from the Patent

Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

23) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-1600.

August, 2007

SD.
S. DEVI, PH.D.
PRIMARY EXAMINER